a.) Amendment to the Specification:

Please amend the paragraph at page 1, lines 15-25 to read as follows.

Bicyclic compounds containing a pyrimidine skeleton in the structure thereof are disclosed as an antipsychotic agent in WO97/47601; as a metabotropic glutamate receptor 1 (mGluR1) antagonist in WO2001/32632; as a glycogen synthase kinase 3 (GSK3) inhibitor in WO2001/44246; as a protein kinase inhibitor in WO2002/22601, WO2002/22602, WO2002/22604, WO2002/22606, WO2002/22607, WO2002/50065 and WO2002/62789; as a modulator of CC chemokine receptor 4 (CCR4) function in WO2002/30358 and US Published Patent Application ~~No. 2003/087513;~~ No. 2003/0173524; and as a phosphodiesterase 7 (PDE7) inhibitor in WO2002/87513, respectively.

Please amend the paragraphs at page 17, lines 8-10 to read as follows.

~~In the definitions of respective groups in Formula (I); and~~

In the definitions of respective groups in Formulae (I) to (IV),

Please amend the paragraph starting at page 18, line 17 and ending at page 19, line 3 to read as follows.

(viii) Examples of the heteroaromatic group and the heteroaromatic moiety of the heteroaromatic-substituted alkyl include five- or six-membered monocyclic heteroaromatic groups containing at least one atom selected from a nitrogen atom, an oxygen atom and a sulfur atom; and condensed bicyclic or tricyclic heteroaromatic groups in which 3- to 8-membered rings are condensed and containing at least one atom selected

from a nitrogen atom, an oxygen atom and a sulfur atom. Specific examples thereof include pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, benzimidazolyl, 2-oxobenzimidazolyl, benzotriazolyl, benzofuryl, benzothienyl, purinyl, benzoxazolyl, benzothiazolyl, benzodioxolyl, indazolyl, indolyl, isoindolyl, ~~purinyl,~~ quinolyl, isoquinolyl, phthalazinyl, naphthyridinyl, quinoxalinyl, pyrrolyl, pyrazolyl, quinazolinyl, cinnolinyl, triazolyl, tetrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thienyl, furyl and the like.

Please amend the paragraph at page 45, lines 7-11 to read as follows:

Examples of the sulfonyl halide are methanesulfonyl chloride, ~~benzenesulsulfonyl chloride~~ benzenesulfonyl chloride and p-toluenesulfonyl chloride, and examples of the sulfonic anhydride are methanesulfonic anhydride and toluenesulfonic anhydride, of which methanesulfonyl chloride is preferred.

Please amend the paragraph starting at page 49, line 29 and ending at page 50, line 2 to read as follows:

The reaction is carried out at temperatures from 0°C to 150°C and preferably from 0°C to 50°C, generally for 1 hour to 48 hours.

~~is not rendered.~~

Please amend the paragraphs starting at page 384, line 19 and ending at page 385, line 2 to read as follows:

In the same way as Reference Example 28, 8-(2-morpholin-2-ylethyl)-1,4-dioxa-8-azaspiro[4,5]decane hydrochloride was prepared from 2-(4-benzylmorpholin-2-yl) acetate and 1,4-dioxa-8-azaspiro[4,5]decane.

Reference Example 31: Syntheses of ~~2-[2-(4-fluoropiperidyl)ethyl]morpholine~~ 2-[2-(4-fluoropiperidino)ethyl]morpholine hydrochloride and ~~2-[2-(4,4-difluoropiperidyl)ethyl]morpholine~~ 2-[2-(4,4-difluoropiperidino)ethyl]morpholine hydrochloride for use in the syntheses of Compounds 20-16 through 20-21

In the same way as Reference Example 28, ~~2-[2-(4-fluoropiperidyl)ethyl]morpholine~~ 2-[2-(4-fluoropiperidino)ethyl]morpholine hydrochloride and ~~2-[2-(4,4-difluoropiperidyl)ethyl]morpholine~~ 2-[2-(4,4-difluoropiperidino)ethyl]morpholine hydrochloride were prepared from 2-(4-benzylmorpholin-2-yl) acetate, and 4-fluoropiperidine and 4,4-difluoropiperidine, respectively.

Please amend the paragraphs starting at page 414, line 2 and ending at page 416, line 4 to read as follows.

Initially, 1-[6-tert-butoxycarbonyl-4-(2,4-dichlorobenzylamino)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-2-yl]piperidine-4-carboxylic acid (1.30 g, 2.50 mmol) was prepared in the same way as Reference Example 8 from 2,4-dichloro-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidine hydrochloride prepared according to Reference Example 1, except for using 2,4-dichlorobenzylamine instead of 2-chloro-4-

fluorobenzylamine. Next, 1-[6-tert-butoxycarbonyl-4-(2,4-dichlorobenzylamino)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-2-yl]piperidine-4-carboxylic acid was dissolved in chloroform (50 mL), and the solution was mixed with a solution of N-hydroxybenzotriazole in chloroform-tetrahydrofuran (2:1) (0.25 mol/L, 20 mL), a solution of 2-(4-morpholino)ethylamine in chloroform (1.00 mol/L, 8.0 mL) and N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide polymer-bound (7.0 g), followed by stirring at 50°C for eighteen hours. After checking the completion of the reaction by thin layer chromatography, the solid was separated from the reaction mixture by filtration, and the filtrate was concentrated. The residue was purified by silica gel column chromatography (ethyl acetate:n-hexane:triethylamine=10:10:1) and thereby yielded tert-butyl 4-(2,4-dichlorobenzylamino)-2-[4-(2-morpholin-4-ylethylcarbamoyl)~~piperidyl~~]piperidino]-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidine-6-carboxylate (0.80 g, in a yield of 50%).

Process Step 2

Tert-butyl 4-(2,4-dichlorobenzylamino)-2-[4-(2-morpholin-4-ylethylcarbamoyl)~~-piperidyl~~]piperidino]-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidine-6-carboxylate prepared according to Process Step 1 (0.80 g) was dissolved in dichloromethane (50 mL), and the solution was mixed with trifluoroacetic acid (10 mL), followed by stirring at room temperature for one hour. The reaction mixture was concentrated under reduced pressure, the residue was dissolved in ethyl acetate, and the solution was mixed with an aqueous sodium hydroxide solution (1.0 mol/L), followed by stirring. The reaction mixture was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, were dried over anhydrous magnesium sulfate, and the solvent was distilled off, to thereby yield 4-(2,4-

dichlorobenzylamino)-2-[4-(2-morpholin-4-ylethylcarbamoyl)~~-piperidyl~~]piperidino]-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidine (0.56 g, in a yield of 84%).

Process Step 3

4-(2,4-Dichlorobenzylamino)-2-[4-(2-morpholin-4-ylethylcarbamoyl) ~~piperidyl~~]piperidino]-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidine prepared according to Process Step 2 (0.56 g, 1.1 mmol) was dissolved in chloroform, and the solution was mixed with N-hydroxybenzotriazole (161 mg), 1-hydroxycyclopropanecarboxylic acid (210 mg) and N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide polymer-bound (2.9 g), followed by stirring at 50°C for one hour. After checking the completion of the reaction by thin layer chromatography, the solid was separated from the reaction mixture by filtration, and the filtrate was concentrated. The residue was purified by silica gel column chromatography (ethyl acetate:triethylamine=10:1), and ethyl acetate was added for crystallization. The precipitated crystals were collected by filtration, were dried under reduced pressure and thereby yielded Compound 14-13 (298 mg, 44%).

Please amend the paragraphs starting at page 443, line 22 and ending at page 444, line 3 to read as follows.

Compound 21-3 was prepared in the same way as Example 31, except for allowing 4-(2,4-dichlorobenzylamino)-2-[4-(1-methylpiperidin-3-yloxy)~~piperidyl~~] piperidino]-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidine prepared in the same way as Example 4 to react with ethyl isocyanate.

Example 106: Synthesis of Compound 21-4

Compound 21-4 was prepared in the same way as Example 31, except for allowing 4-(2,4-dichlorobenzylamino)-2-[4-(1-methylpiperidin-4-yloxy)~~-piperidyl]~~ piperidino]-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidine prepared in the same way as Example 4 to react with ethyl isocyanate.

Please amend the paragraph at page 447, lines 1-8 to read as follows:

Compounds 23-3 through 23-5 were prepared in the same way as Process Step 2 of Example 109, except for allowing 4-(2-chloro-4-fluorobenzylamino)-6-(cyclopropylcarbonyl)-2-(4-formylphen-1-yl)-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidine prepared according to Process Step 1 of Example 109 to react with piperidine, 4-hydroxypiperidine or 1-methyl-4-methylaminopiperidine, respectively, instead of pyrrolidine used in Process Step 2 of ~~Example 110~~ Example 109.